

Differences Between Squamous Cell Carcinoma and Keratoacanthoma in Angiotensin Type-1 Receptor Expression

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ABSTRACT

Introduction

Angiotensin II (AngII) of the renin-angiotensin system is the active biological peptide that regulates blood pressure and salt and water homeostasis. AngII exerts its actions by binding the specific receptors. There are two major subtypes of the angiotensin receptors; type 1 (AT1) and type 2 (AT2). In the human skin, little is known about the expression of the angiotensin receptors. We studied the expression of angiotensin receptors in the normal human skin. Based on the results, we studied the expression of AT1 in squamous cell carcinoma (SCC) and keratoacanthoma (KA). It is sometimes difficult to distinguish SCC of the skin from KA because of the histological resemblance of these tumors. At present, few methods enable it possible to distinguish SCC from KA. Our experiments revealed differences between SCC and KA in AT1 expression.

Materials and Methods

A total of fifty cases of SCC of the skin and fourteen cases of SCC of the lip were selected from a consecutive series of sixty-nine cases diagnosed and treated for SCC at Yamagata University Hospital, Japan between 1978-1999. All twenty-two cases that were diagnosed and treated for KA at the hospital between 1978-1999 were also studied. Normal back skin from a 38-year-old Japanese woman, normal lip from a 64-year-old Japanese man, and normal brain tissue from a 33-year-old man were used as normal controls. Five- μ m-thick paraffin-embedded tissue sections were offered for hematoxylin and eosin stain and immunohistochemical study using the labeled streptavidin-biotin method. The primary antibodies used in this study were anti-angiotensin type-1 and type-2 receptor antibodies.

In cases of SCC of the skin, SCC of the lip, and KA, the percentage of AT1-positive tumor cells of all neoplastic cells in the section was estimated and graded into one of three categories: low (<35%); intermediate (35 to 75%); or (c) high (>75%). Among the cases that were graded high, there was a group of cases that showed a distinct staining

pattern. In this pattern, 1 to 2 layers of the tumor cells that were located at the periphery of the tumor nest stained negatively. This pattern was termed as negative periphery and was graded as one category independent of the other three categories that showed no particular arrangement of AT1-positive cells.

Results

In the interfollicular epidermis of normal human skin, the suprabasal epidermis stained positive with AT1, but the basal layer was negative. As to the infundibulum of the hair follicle, the suprabasal layers of the outer root sheath were all positive. The basal layer of the outer root sheath was negative. In the vermilion border of normal lip, unlike the normal epidermis, the upper two to three layers of the epithelium stained positive with AT1, but the other layers of the epithelium including the basal layer were negative. In SCC of the skin, high, intermediate, and low levels of AT1 were observed in thirty-seven (74.0%), seven (14.0%), and two cases (4.0%), respectively. Four cases (8.0%) showed negative periphery pattern. In KA, seventeen cases (77.3%) showed a negative periphery pattern. In SCC of the lip, high, intermediate, and low levels of AT1 were observed in three (21.4%), three (21.4%), and six cases (42.9%), respectively. Two cases (14.3%) showed a negative periphery pattern. All specimens were negative with anti-AT2 antibody.

Discussion

Immunohistochemical study demonstrated the expression of AT1 in the normal human skin and the skin tumors. SCC of the skin is generally believed to originate from the normal squamous cells which are located in the suprabasal epidermis. In SCC, 74.0% of the cases were graded as high. This result seem to reflect the belief of suprabasal origin of SCC. On the other hand, KA, which is a benign skin tumor, often resembles well- or moderately differentiated SCC clinically and histologically. In some cases, KA shows a greater degree of nuclear atypia than do some SCCs, and this makes the differentiation of two diseases very difficult. It is generally believed that KA has its origin in the infundibulum of one or several hair follicles. In KA, 77.3% of the cases were graded as negative periphery. This result seem to reflect the infundibular origin of KA. The results of immunostaining of SCC and KA demonstrated a striking contrast. Our study indicate that immunohistochemical study of the expression of AT1 assists one to distinguish SCC from KA. In SCC of the lip, the percentage of AT1-positive cells of the tumor cells is low compared to that SCC of the skin and this result may reflect less immunoreactivity with AT1 of the normal lip epithelium. These observations suggest that the immunohistochemical study of AT1 is useful to distinguish SCC from KA. Studying the role and distribution of AT1 may help in understanding the pathophysiology of the skin.